the target nucleic-acid polymer complementary to the primer-extension-initiation 3'-end nucleotide of the detection-primer nucleotide sequence defining a primer-end complement nucleotide. The primer-hybridizing nucleotide sequence of the target nucleic-acid polymer extends towards the 3' end of the target polymer from the primer-end complement nucleotide. The primer-end complement nucleotide is located in the target polymer at a position 3'-ward of the predetermined target position. The position of the primer-end complement nucleotide is subject to a constraint that no nucleotide of the same type as the one or more specific nucleotides to be detected be located in the target polymer in any position between the position of the primer-end complement nucleotide and the predetermined target position.

The reagent kit of the invention further includes an enzymatic polymerizing agent.

The reagent kit of the invention also includes an admixture of nucleoside triphosphates. In a first aspect, the admixture of nucleoside triphosphates includes at least one deoxynucleotide and at least two chain-terminating nucleotide analogues. At least one deoxynucleotide in such first aspect comprises a detectable label or an attachment moiety capable of binding a detectable label. In a second aspect, the admixture of nucleoside triphosphates includes at least one deoxynucleotide and at least one chain-terminating nucleotide analogue. At least one chain-terminating nucleotide analogue in such second aspect comprises a detectable label or an attachment moiety capable of binding a detectable label. Each deoxynucleotide of the admixture of nucleoside triphosphates is complementary to a nucleotide which differs from any nucleotide to which a chain-terminating nucleotide analogue of the admixture is complementary.

In use, the detection primer of the reagent kit of the invention can hybridize to the target nucleic-acid polymer at the primer-hybridizing nucleotide sequence and form a detection-primer extension product by an enzyme-catalyzed primer-extension reaction to permit the presence or absence of a specific nucleotide at the predetermined target position to be detected by detecting

the presence or absence of a corresponding detectable label in association with the detection-primer extension product.

B. Summary of the Outstanding Office Action

Claims 51 through 53 inclusive, 63, 67, and 71 through 75 inclusive were rejected in the outstanding Office Action under 35 U.S.C. § 103 as unpatentable over United States patent No. 5,310,893 to Erlich *et al.* ("the Erlich *et al.* '893 patent") in view of Unites States patent No. 4,683,202 to Mullis ("the Mullis '202 patent).

Claims 51, 53 and 72 through 75 inclusive were rejected under 35 U.S.C. § 103(a) in the Office Action of 25 April 2002 as unpatentable over United States patent No. 4,656,127 to Mundy ("the Mundy '127 patent").

Claims 56 and 57 were rejected in the outstanding Office Action under 35 U.S.C. § 103 as unpatentable over the Mundy '127 patent in view of a publication by Emi *et al.* in *Genonics,* volume 3, pages 373-379 (1988) ("the Emi *et al.* publication")

Claim 59 was rejected under 35 U.S.C. § 103 as unpatentable in the outstanding Office Action over a publication by Saiki *et al.* in *Nature*, volume 324, pages 163-166 (1986) ("the Saiki *et al.* publication").

Claim 62 was rejected in the Office Action of 25 April 2002 under 35 U.S.C. § 103 as unpatentable over the Mundy '127 patent in view of a publication of Farr *et al.* in *PNAS,* volume 85, pages 1629-1633 (1988) ("the Farr *et al.* publication").

C. Summary of the Present Amendments and Request for Reconsideration

Claims 51 through 53 inclusive, 56, 57, 59, 62, 63, 67, and 71 through 75 inclusive have been canceled without prejudice. The applicants expressly reserve the right to prosecute claims to subject matter of any or all of the cancelled claims 51 through 53 inclusive, 56, 57, 59, 62, 63, 67, and 71 through 75 inclusive in one or more continuation, divisional, continued prosecution, or other continuing application.

New claims 97 through 116 inclusive have been added in the present response. It is submitted that new claims 97 through 116 inclusive do not constitute new matter.

Reconsideration of the subject application as amended above in light of the comments below is respectfully requested.

D. The Rejections Under 35 U.S.C. § 103

D.1. The Erlich *et al.* '893 Patent in View of the Mullis '202 Patent

The Erlich *et al.* '893 patent discloses a process for determining the genotype of an individual with respect to alleles at the HLA DP locus. The process involves amplifying nucleic acid with a polymerase chain reaction method using primers specific for a second exon of the DPalpha and DPbeta genes. According to column 8, lines 22 through 27 of the Erlich *et al.* '893 patent, template extension of primers in a polymerase chain reaction is catalyzed by a polymerizing agent in the presence of four deoxyribonucleoside triphosphates (dATP, dGTP, dCTP, and dTTP).

New independent claims 97 and 107 of the subject application are each directed to a reagent kit including a detection primer of specified characteristics, an enzymatic polymerizing agent, and an admixture of nucleoside triphosphates. In each of claims 97 and 107, the admixture of nucleoside triphosphates is specified to include at least one chain-terminating nucleotide analogue. It is submitted that the presence of a chain-terminating nucleotide analogue renders the admixture essentially useless for carrying out a conventional polymerase chain reaction, since the chain extension reaction would terminate wherever a chain-terminating nucleotide analogue was incorporated in a nucleotide chain.

The Erlich *et al.* '893 patent discloses at column 9, lines 6 through 16 that one use for the polymerase chain reaction for the purposes of the patent is for determining the nucleotide sequence of allelic variants which exist in the HLA-DP region. According to the '893 patent, DPalpha and DPbeta genes may be amplified and nucleotide sequences of polymorphic target regions determined.

New independent claim 97 is directed to a reagent kit which includes a detection primer of certain specified characteristics, an enzymatic polymerizing agent, and an admixture of nucleoside triphosphates including at least one deoxynucleotide and at least two chain-terminating nucleotide analogues. At least one deoxynucleotide of the admixture comprises a detectable label or an attachment moiety capable of binding a detectable label. It is submitted that a person of ordinary skill in the art, as of the effective filing date of the subject application, would not have attempted to use a reagent kit as defined in new claim 97 of the subject application for determining the nucleotide sequence of allelic variants in attempting to carry out the procedures of the Erlich *et al.* '893 patent.

New independent claim 107 of the subject application is directed to a reagent kit comprising a detection primer of specified characteristics, an enzymatic polymerizing agent, and

an admixture of nucleoside triphosphates including at least one deoxynucleotide and at least one chain-terminating nucleotide analogue. At least one chain-terminating analogue of the admixture of claim 107 comprises a detectable label or an attachment moiety capable of binding a detectable label. Each deoxynucleotide of the admixture of nucleoside triphosphate is specified in claim 107 to be complementary to a nucleotide which differs from any nucleotide to which a chain-terminating nucleotide analogue of the admixture is complementary. It is submitted that a person of ordinary skill in the art as of the effective filing date of the subject application would have not attempted to use a reagent kit as defined in new claim 107 for determining the nucleotide sequence of allelic variants in attempting to practice the procedures of the Erlich *et al.* '893 patent.

For the reasons set forth above, it is submitted that the Erlich *et al.* '893 patent would have neither disclosed nor suggested the subject matter of new independent claims 97 and 107 to a person of ordinary skill in the art as of the effective filing date of the subject application.

The Mullis '202 patent does not cure the infirmities of the Erlich *et al.* '893 patent as a reference against new claims 97 and 107 of the subject application as amended. It is submitted, therefore, that the Erlich *et al.* '893 patent considered alone or in combination with the Mullis '202 patent neither discloses nor suggests the subject matter of new claims 97 and 107.

New claims 98 through 106 inclusive and 108 through 116 inclusive of the application as amended are dependent claims which depend upon new independent claims 97 and 107 and consequently incorporate the limitations of new claims 97 and 107 by reference. The reasoning set forth above concerning distinctions between the Erlich *et al.* '893 patent considered alone or in combination with the Mullis '202 patent and new claims 97 and 107 therefore applies with equal force with respect to new dependent claims 98 through 106 inclusive and 108 through 116 inclusive.

For the reasons set forth above, it is submitted that a rejection of any of new claims 97 through 116 inclusive as unpatentable over the Erlich *et al.* '893 patent alone or in combination with any of the art of record would be unwarranted.

D.2. The Mundy '127 Patent Taken Alone or in View of the Emi *et al.*, the Saiki *et al.*, and the Farr *et al.* Publications

The Mundy '127 patent discloses methods of detecting a mutation of a specific nucleotide base in a target nucleic acid chain. One method of the Mundy '127 patent disclosed at column 3, line 49 through column 4, line 27 comprises hybridizing a labeled probe to the target nucleic acid chain to form a hybrid in which one end of the probe becomes hybridized to the target chain either immediately adjacent to a specific base or a few bases away from the specific base. The hybrid is then admixed with a chain terminating nucleotide compound, optionally in the presence of one or two other different nucleotides, under probe extension conditions to cause the chain terminating nucleotide compound to join to the end of the probe, if the compound is complementary to the specific base. Thereafter, one or more digestion-resistant nucleotide derivatives are admixed with the hybrid under probe extension conditions to render the probe digestion resistant if the probe has not been terminated with a chain-terminating nucleotide compound.

The Mundy '127 patent discloses at column 6, line 67 through column 7, line 6 that it may be possible to use a nucleotide derivative which is labeled. In the parlance of the Mundy '127 patent, a "nucleotide derivative" is a digestion resistant nucleotide moiety. The Mundy '127 patent does not disclose or suggest using a chain-terminating nucleotide compound which has been labeled. The Mundy '127 patent does not disclose or suggest treating a hybrid under probe-

extension conditions with a chain-terminating nucleotide compound and one or more other nucleotides which have been labeled.

New independent claim 97 is directed to a reagent kit which contains, among other things, an admixture of nucleoside triphosphates including at least one deoxynucleotide and at least two chain-terminating nucleotide analogues. At least one deoxynucleotide of the admixture is specified to comprise a detectable label or an attachment moiety capable of binding a detectable label. New independent claim 107 is directed to a reagent kit which includes, among other components, an admixture of nucleoside triphosphates including at least one deoxynucleotide and at least one chain-terminating nucleotide analogue wherein at least one chain-terminating nucleotide analogue comprises a detectable label or an attachment moiety capable of binding a detectable label.

For the reasons set forth above, it is submitted that the Mundy '127 patent would have neither disclosed nor suggested the subject matter of new independent claims 97 and 107 to a person of ordinary skill in the art as of the effective filing date of the subject application.

None of the Emi *et al.* publication, the Saiki *et al.* publication, and the Farr *et al.* publication cures the infirmities of the Mundy '127 patent as a reference against new claims 97 and 107 of the subject application as amended. It is submitted, therefore, that the Mundy '127 patent considered alone, or in any combination with the Emi *et al.*, the Saiki *et al.*, and the Farr *et al.* publications, neither discloses nor suggests the subject matter of new claims 97 and 107.

New claims 98 through 106 inclusive and 108 through 116 inclusive of the application as amended are dependent claims which depend upon new independent claims 97 and 107 and consequently incorporate the limitations of new claims 97 and 107 by reference. The reasoning set forth above concerning distinctions between the Mundy '127 patent considered alone or in

combination with the Emi *et al.*, the Saiki *et al.*, and the Farr *et al.* publications and new claims 97 and 107 therefore applies with equal force with respect to new dependent claims 98 through 106 inclusive and 108 through 116 inclusive.

For the reasons set forth above, it is submitted that a rejection of any of new claims 97 through 116 inclusive as unpatentable over the Mundy '127 patent alone or in combination with any of the art of record would be unwarranted.

E. Conclusion

For the reasons set forth above, it is submitted that the claims of the subject application as amended are patentable over the art of record considered alone or in any combination. Early allowance of the application is therefore earnestly solicited.

Respectfully submitted,

Attorneys for the Applicants

by _____
J. David Ellett, Jr.
Reg. No. 27,875

Telephone No.: (212) 813-1600